Preparation for Term Paper
(Genomic Heritability Calculations)

Review from Barry et al. 2023 (*Figure 1*)

- **Family Based Designs**
  - Twin Studies
  - Extended Twin Design (including other relatives)
- **Genomic Methods: Unrelated Individuals**
  - Linkage Disequilibrium (*LD*) Score Regression
    - Supplemental Materials describe implementation in *LDSC* package (Bulik-Sullivan et al. 2015).
  - Genomic relatedness REstricted Maximum-Likelihood (***GREML***)
    - Part of *GCTA* (Genome-wide Complex Trait Analysis, Yang et al. 2011)
    - *GCTA* Wikipedia Entry
  - LD- and MAF-stratified GREML (*GREML-LDMS*, Yang et al. 2015)
- **Genomic Methods: Related Individuals**
  - *GREML-KIN* (GREML with KINship analysis – Hill et al. 2018, Xia et al. 2016, and/or Zaitlen et al. 2013.
    - On the *GCTA* website, the section for "*GREML in family data*" references Zaitlen et al. 2013.
  - ***Trio-GCTA*** (Eilertsen et al. 2021)
  - Material (or Paternal) GCTA (*M-GCTA*, Qiao et al. 2020)
  - Relatedness Disequilibrium Regression (***RDR***, Young et al. 2018)
    - Supplemental Materials also reference Visscher et al. 2006.
- *Table 1* also describes strengths and limitations, which include the relative estimated contribution of rare variants.
- *Box 1* defines narrow-sense heritability versus broad sense heritability.

Newer/Additional Methods

- *GPLEMMA* (Kerin and Marchini 2020)
  - Cites ***RDR*** publication (Young et al. 2018)
- SAFE-h^2 (Darbani and Nicolaisen 2023)
  - Includes comparisons to *EMMAX* (Kang et al. 2010) and ***LDAK***.
  - *EMMAX* = EMMA eXpeditated, an extension of EMMA (Kang et al. 2008).
  - Two implementations for ***LDAK*** are mentioned. One is within *GCTA*, and the other is described as ***LDAK-Thin*** (Speed et al. 2012).
- The GCTA webpage lists *sBLUP* among available methods, but not necessarily for heritability?
  - sBLUP = Summary-level BLUP
  - Best Linear Unbiased Prediction (BLUP) is referenced in Wang et al. 2019
  - The *rrBLUP* (ridge-regression BLUP) R-package is a dependency for the *Bloom et al. 2019* code (imported in *mapping.R*, for example).

- While not an additional method, Tang et al. 2022 is an additional review on the general topic.
  - Includes descriptions of additional methods.
- Srivastava et al. 2023 is another such review.
  - Describes *REML* (REstricted Maximum Likelihood, with applications in Lee et al. 2006 and Yang et al. 2010) for individual-level data, before listing assumptions for ***GREML*** versus ***LDAK***.
- *Bloom et al. 2019* references de los Campos et al. 2015 ("*Genomic Heritability: What Is It?*")

- Evans et al. 2018 provides a comparison of different methods.
  - It looks like there is noticeable emphasis on implementation of *GREML* and *LDAK* methods.

Methods for Additional Focus

- Genomic relatedness REstricted Maximum-Likelihood (***GREML***)
  - Part of *GCTA* (Genome-wide Complex Trait Analysis, Yang et al. 2011)
  - Can be cited as Yang et al. 2010
- Linkage-Disequilibrium Adjusted Kinships (***LDAK,*** Speed et al. 2012).
- Relatedness Disequilibrium Regression (***RDR***, Young et al. 2018)
- ***Trio-GCTA*** (Eilertsen et al. 2021)
- "*GREML-WGS*" (Wainschtein et al. 2022)
  - Young 2019 used "*GREML-WGS*" to describe this method.
    - This is possible due to the difference in date for the first preprint (**2019**) versus the peer-reviewed version (**2022**).
  - Plots in the publication describe using "*GREML-LDMS*", but the data is Whole Genome Sequencing data (where I would expect that there should be no imputation).

Previous Related Discussions

- I have a *journal comment/question* for Young 2019, which was referenced in the Barry et al. 2023 review.
  - This was in turn referenced in a *preprint comment* for Dolan et al. 2019, which specifically references ***RDR*** (in reference to *Young 2019* comment/question above) as well as ***heritability***.
- I have *preprint comment* on an article titled "*Recovery of trait heritability from whole genome sequence data*" (with a later peer-reviewed version published in Wainschtein et al. 2022).
- As might be expected, "*heritability*" is mentioned in the earlier *preprint comment* for the *Bloom et al. 2019* data that I am (partially) re-analyzing.

- Because data analysis was not performed, it may be somewhat off topic. However, there was mention to interpretation of heritability in a *preprint comment* on Lowes et al. 2022.

- While not exactly about heritability, I have a *preprint comment* related to predicting height for Thompson et al. 2022.
- Height is also briefly mentioned in a *Disqus comment* for Marnetto et al. 2020, even if not currently visible on the journal website?.

Additional Reviews
(*referenced by Barry et al. 2023*)

- In addition to the Visscher et al. 2010 height GWAS article mentioned in the Height QTL Notes, Barry et al. 2023 reference a review related to heritability and genomics in Visscher et al. 2008.
- A review by Mayhew et al. 2017 is also referenced.

- Yang et al. 2017 includes a figure related to estimation of height heritability with *different methods*.

- Young 2019 includes a table showing variation in heritability values for height (with *different methods* and in different cohorts).

- Zhu and Zhou 2020 is another cited review.